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UNUNNNANCCNNNNNNNN (SEQ ID NO:415) or NNUNNNNNNNNGAUCNUNNNNGAUNC
UUUNUNNNACCNNNNNNNN (SEQ ID NO:416).

83. (Amended twice) A purified and isolated RNA fragment that is conserved across at least two species comprising the sequence NNUNNNNNNNNGAUCNUNNNNGAUNCUUUNUNNN ANNCCNNNNNNNN (SEQ ID NO:20), NNUNNNNNNNNGAUCNUNNNNGAUNCUUUNUN NNANCCNNNNNNNN (SEQ ID NO:415) or NNUNNNNNNNNGAUCNUNNNNGAUNCUUUN UNNNACCNNNNNNNN (SEQ ID NO:416).

REMARKS

Claims 64, 71, 78, and 81-83 have been amended. Substitute pages 1-129 are provided to comply with the Sequence Rules set forth in 37 CFR §§1.821-1.825, formatted under the new rules for submitting Sequence Listings. The claims and specification have been amended to further clarify "N(or absent)" phrases in regard to the sequence identifiers, as requested by the Examiner. In particular, sequence identifiers have been added for each of the individual sequences disclosed within a sequence reciting "N(or absent)." Support for the amendments can be found throughout the application as originally filed. No new matter has been added. In addition, enclosed herewith is a Statement to Support Filing and Submission of DNA/Amino Acid Sequences in Accordance with 37 CFR §§1.821-1.825 and a computer readable form (CRF). The contents of the paper copy of the Sequence Listing and computer readable copy of the Sequence Listing, submitted in accordance with 37 CFR §1.821(c) and (e), are the same.

The Examiner has mistakenly restricted claims 1-113 into eight groups. Group I contains claims 1-20, 31, 33 and 34 drawn to a portion of interleukin-2 RNA. Group II contains claims 21-30 and 32 drawn to *in silico* portion of interleukin-2 RNA. Group III contains claims 35-48, 56, 58 and 59 drawn to a portion of interleukin-2 RNA. Group IV contains claims 49-55 and 57 drawn to *in silico* portion of interleukin-2 RNA. Group V contains claims 60-73, 81 and 83-86 drawn to a portion of interleukin-2 RNA. Group VI contains claims 74-80 and 82 drawn to *in silico* portion of interleukin-2 RNA. Group VII contains claims 87-100, 108 and 110-113 drawn to a portion of

interleukin-2 RNA. Group VIII contains claims 74-80 and 82 drawn to *in silico* portion of interleukin-2 RNA. Applicants elect Group VII, containing claims 87-100, 108 and 110-113 with traverse.

As a preliminary matter, Applicants believe that Group VIII should recite claims 101-107 and 109 rather than 74-80 and 82, which is duplicative of the claims of Group VI.

§803 of the M.P.E.P. mandates two criteria for a proper requirement for restriction: 1) the inventions must be independent or distinct; **and** 2) there must be a serious burden on the examiner. The Office Action mistakenly asserts that Groups I, III, V and VII are unrelated because they are not disclosed as capable of use together and they have "different modes of operation, different functions, or different effects" because they have different molecular structures and nucleotide sequences. That the RNA molecules have different molecular structures and nucleotide sequences does not mean that they have "different modes of operation, different functions, or different effects." Indeed, the RNA molecules recited in the claims of Groups I, III, V and VII are all portions of interleukin-2. In addition, Applicants use the RNA molecules for the same purpose. Significantly, the Office Action does not identify the "different modes of operation, different functions, or different effects." Further, taking the Examiner's statement to its logical conclusion would result in a most unwarranted ten-way restriction requirement for ten oligonucleotides differing from each other by only one nucleotide (i.e., each would have a different molecular structure and nucleotide sequence). Because the RNA molecules recited in the claims of Groups I, III, V and VII are derived from the same biomolecule and are used by Applicants for the same purposes, the RNA molecules are clearly related.

For purposes of initial requirement, a serious burden on the examiner may be *prima facie* shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in M.P.E.P. §808.02. Significantly, the Examiner has not met the *prima facie* burden. Contrary to the assertions otherwise in the Office Action, separate status in the art is not shown by different classification or divergent subject matter. Indeed, each of Groups I, III, V and VII are within the same class, class 536, and the same subclasses, subclasses 23.1 and 24.5. Thus, separate classification for Groups I, III, V, and VII does not exist. Further, the Examiner has not shown separate status in the art or a requirement for a different field

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of search. Indeed, each of the RNA molecules in groups I, III, V, and VII are derived from the same biomolecule, interleukin-2. Thus, the same field of search is required for each of groups I, III, V and VII due to their same status in the art. Significantly, the Examiner only provides conclusory statements without any reasoning to support the same. Accordingly, there is no serious burden to examine the claims of groups I, III, V, and VII together, and Applicants respectfully request reconsideration of the restriction requirement. ✓

Applicants submit that the present response is complete and complies with the requirements of 35 U.S.C. §121. In addition, Applicants submit that, at a minimum, claims of Groups I, III, V and VII must be considered in the present application without restriction.

The Examiner is invited to contact Applicants' undersigned representative at (215) 564-8906 if there are any questions regarding Applicants' claimed invention. Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment.

The attached page is captioned "Version with markings to show changes made."



Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE**In the Application:**

Pages 1-119 of the application containing the Sequence Listing have been deleted and replaced with new pages 1-129 containing the amended Sequence Listing.

In the Specification:

Paragraph beginning at page 144, line 3 of the specification has been amended as follows:

In other preferred embodiments, the nucleic acid fragment comprise the consensus sequence [(SEQ ID NO:1) NNNNCNNNNNNN(or absent)NUNNANNNNNNNN] NNNNCN
NNNNNNUNNANNNNNNNN (SEQ ID NO:1) or NNNNCNNNNNNNUNNANNNNNNNN
(SEQ ID NO:384) and wherein the sequence has a first double stranded region, an internal loop region, a second double stranded region and an end loop region. In other preferred embodiments, an *in silico* representation of a nucleic acid fragment that is conserved across at least two species comprises the consensus sequence [NNNNCNNNNNNN(or absent)NUNNANNNNNNNN]
NNNNCNNNNNNNUNNANNNNNNNN or NNNNCNNNNNNNUNNANNNNNNNN. In other preferred embodiments, a purified and isolated nucleic acid fragment that is conserved across at least two species comprises the sequence [NNNNCNNNNNNN(or absent)NUNNANNNNNNNN]
NNNNCNNNNNNNUNNANNNNNNNN or NNNNCNNNNNNNUNNANNNNNNNN. In other preferred embodiments, a purified and isolated nucleic acid fragment comprises the human sequence (SEQ ID NO:2) UUUACAACAUAUUCUAGUUUACAGAAAAAUC. In other preferred embodiments, an *in silico* representation of a nucleic acid fragment comprises the human sequence UUUACAACAUAUUCUAGUUUACAGAAAAAUC.

Paragraph beginning at page 145, line 19 of the specification has been amended as follows:

In other preferred embodiments, the nucleic acid comprises the consensus sequence [(SEQ ID NO:3) NNNNANAUGGGN(or absent)N(or absent)N(or absent)UCACANNUAN(or absent) CUGUGUUCCUAUGGAAACUN(or absent)N(or absent)UUN] NNNNANAUGGGNNNUCA
CANNUANCUGUGUUCCUAUGGAAACUNNUUN (SEQ ID NO:3), NNNNANAUGGGNN

NUCACANNUACUGUGUCCUAUGGAAACUNNUUN (SEQ ID NO:385), NNNNANAUGG
GNNNUCACANNUACUGUGUCCUAUGGAAACUNUUN (SEQ ID NO:386), NNNNAN
AUGGGNNNUCACANNUACUGUGUCCUAUGGAAACUUUN (SEQ ID NO:387), NNNNA
NAUGGGNNNUCACANNUANCUGUGUCCUAUGGAAACUNUUN (SEQ ID NO:388), NNN
NANAUGGGNNNUCACANNUANCUGUGUCCUAUGGAAACUUUN (SEQ ID NO:389),
NNNNANAUGGGNNNUCACANNUANCUGUGUCCUAUGGAAACUNNUUN (SEQ ID
NO:390), NNNNANAUGGGNNNUCACANNUACUGUGUCCUAUGGAAACUNNUUN (SEQ
ID NO:391), NNNNANAUGGGNNNUCACANNUACUGUGUCCUAUGGAAACUNUUN (SEQ
ID NO:392), NNNNANAUGGGNNNUCACANNUACUGUGUCCUAUGGAAACUUUN (SEQ
ID NO:393), NNNNANAUGGGNNNUCACANNUANCUGUGUCCUAUGGAAACUNUUN
(SEQ ID NO:394), NNNNANAUGGGNNNUCACANNUANCUGUGUCCUAUGGAAACUUUN
(SEQ ID NO:395), NNNNANAUGGGNUCACANNUANCUGUGUCCUAUGGAAACUNNU
UN (SEQ ID NO:396), NNNNANAUGGGNUCACANNUACUGUGUCCUAUGGAAACUNN
UUN (SEQ ID NO:397), NNNNANAUGGGNUCACANNUACUGUGUCCUAUGGAAACUN
UUN (SEQ ID NO:398), NNNNANAUGGGNUCACANNUACUGUGUCCUAUGGAAACUU
UN (SEQ ID NO:399), NNNNANAUGGGNUCACANNUANCUGUGUCCUAUGGAAACUN
UUN (SEQ ID NO:400), NNNNANAUGGGNUCACANNUANCUGUGUCCUAUGGAAACUU
UN (SEQ ID NO:401), NNNNANAUGGGUCACANNUANCUGUGUCCUAUGGAAACUNNU
UN (SEQ ID NO:402), NNNNANAUGGGUCACANNUACUGUGUCCUAUGGAAACUNNUU
N (SEQ ID NO:403), NNNNANAUGGGUCACANNUACUGUGUCCUAUGGAAACUNUUN
(SEQ ID NO:404), NNNNANAUGGGUCACANNUACUGUGUCCUAUGGAAACUUUN (SEQ
ID NO:405), NNNNANAUGGGUCACANNUANCUGUGUCCUAUGGAAACUNUUN (SEQ
ID NO:406), or NNNNANAUGGGUCACANNUANCUGUGUCCUAUGGAAACUUUN (SEQ
ID NO:407) and having a first double stranded region, a first internal loop region, a second double stranded region, a second internal loop region, a third double stranded region and an end loop region.

In other preferred embodiments, a purified and isolated nucleic acid fragment comprises the human sequence (SEQ ID NO:4) UAGGAUAUGGGUCACACUUAUCUGUGUCCUAUGGAAACUA

UUUG. In other preferred embodiments, a purified and isolated nucleic acid fragment comprises the mouse sequence (SEQ ID NO:5) UAGGAGAUGGGGGGUCACACUUACUGUGUUCCUAUGGAAACUUUG. In other preferred embodiments, a purified and isolated nucleic acid fragment comprises the rat sequence (SEQ ID NO:6) UAGGAGAUGGGGGGUCACACUUACUGUGUUC CUAUGAAACUUUUG.

Paragraph beginning at page 146, line 26 of the specification has been amended as follows:

In other preferred embodiments, a nucleic acid comprises the consensus sequence [(SEQ ID NO:7) AUGGGN(or absent)N(or absent)N(or absent)UCACANNUAN(or absent)CU GUGUUCCUAU] AUGGGNNNUCACANNUANCUGUGUUCCUAU (SEQ ID NO:7), AUGG GNNNUCACANNUACUGUGUUCCUAU (SEQ ID NO:408), AUGGGNNNUCACANNUANC UGUGUUCCUAU (SEQ ID NO:409), AUGGGNNNUCACANNUACUGUGUUCCUAU (SEQ ID NO:410), AUGGGNUCACANNUANCUGUGUUCCUAU (SEQ ID NO:411), AUGGGNU CACANNUACUGUGUUCCUAU (SEQ ID NO:412), AUGGGUCACANNUANCUGUGUUC CUAU (SEQ ID NO:413), or AUGGGUCACANNUACUGUGUUCCUAU (SEQ ID NO:414) and having a first double stranded region, an internal loop region, a second double stranded region and an end loop region. A purified and isolated nucleic acid fragment comprising the human sequence (SEQ ID NO:8) AUGGGUCACACUUAUCUGUGUUCCUAU. In other preferred embodiments, a purified and isolated nucleic acid fragment comprising the mouse sequence (SEQ ID NO:9) AUGGGGGGUCACACUUACUGUGUUCCUAU. In other preferred embodiments, a purified and isolated nucleic acid fragment comprising the rat sequence (SEQ ID NO:10) AUGGGGGGUCACACUUACUGUGUUCCUAU.

Paragraph beginning at page 151, line 16 of the specification has been amended as follows:

In other preferred embodiments, a nucleic acid comprising the consensus sequence [(SEQ ID NO:20) NNUNNNNNNNGAUCNUNNNNNGAUNCUUUNUNNNAN(or absent)N(or absent)C CNNNNNNN] NNUNNNNNNNGAUCNUNNNNNGAUNCUUUNUNNNANCCNNNNNNNN (SEQ ID NO:20), NNUNNNNNNNGAUCNUNNNNNGAUNCUUUNUNNNANCCNNNNNNNN

(SEQ ID NO:415), or NNUNNNNNNNGAUCNUNNNNNGAUNCUUUNUNNNNACCNNNNNNNN (SEQ ID NO:416) and having a first double stranded region, a first internal loop region, a second double stranded region, and a first end loop region, a third double stranded region, and a second end loop region. In other preferred embodiments, a purified and isolated nucleic acid fragment comprising the human sequence (SEQ ID NO:21) UAUAAUAUGGAUCUUUAUGAUUCUUUUUGUAAGCCCUAGGGGC. In other preferred embodiments, a purified and isolated nucleic acid fragment comprising the mouse sequence (SEQ ID NO:22) GAUAAUAUGGAUCUUUAAAGAUUCUUUUUGUAAGCCCCAAGGGC. In other preferred embodiments, a purified and isolated nucleic acid fragment comprising the rat sequence GAUAAUAUGGAUCUUUAAAGAUUCUUUUUGUAAGCCCCAAGGGC.

In the Claims:

Claims 64, 71, 78, and 81-83 have been amended as follows:

64. (Amended) The RNA of claim 60 wherein said nucleotides forming said first side of said third stem region are of the sequence [N(or absent)N(or absent)CC,] NNCC, GCCC, or CC and said nucleotides forming said second side of said third stem region are of the sequence NNNN, GGGC, or GCGU.

71. (Amended) The RNA of claim 67 wherein said nucleotides forming said first side of said third stem region are of the sequence [N(or absent)N(or absent)CC,] NNCC, GCCC, or CC and said nucleotides forming said second side of said third stem region are of the sequence NNNN, GGGC, or GCGU.

78. (Amended) The RNA of claim 74 wherein said nucleotides forming said first side of said third stem region are of the sequence [N(or absent)N(or absent)CC,] NNCC, GCCC, or CC and said nucleotides forming said second side of said third stem region are of the sequence NNNN, GGGC, or GCGU.

81. (Amended twice) An RNA comprising the consensus sequence [NNUNNNNNNNGAUCNUNNNNNGAUNCUUUNUNNNAN(or absent)N(or absent)CCNNNNNNN (SEQ ID NO:20)] NNUNNNNNNNGAUCNUNNNNNGAUNCUUUNUNNNANCCNNNNNNN (SEQ ID NO:20), NNUNNNNNNNGAUCNUNNNNNGAUNCUUUNUNNNANCCNNNNNNN (SEQ ID NO:415) or NNUNNNNNNNGAUCNUNNNNNGAUNCUUUNUNNNACCNNNNNNN (SEQ ID NO:416) and having a first double stranded region, a first internal loop region, a second double stranded region, and a first end loop region, a third double stranded region, and a second end loop region.

82. (Amended twice) An *in silico* representation of an RNA fragment that is conserved across at least two species comprising the sequence [NNUNNNNNNNGAUCNUNNNNNGAUNCUUUNUNNNAN(or absent)N(or absent)CCNNNNNNN (SEQ ID NO:20)] NNUNNNNNNNGAUCNUNNNNNGAUNCUUUNUNNNANCCNNNNNNN (SEQ ID NO:20), NNUNNNNNNNGAUCNUNNNNNGAUNCUUUNUNNNANCCNNNNNNN (SEQ ID NO:415) or NNUNNNNNNNGAUCNUNNNNNGAUNCUUUNUNNNACCNNNNNNN (SEQ ID NO:416).

83. (Amended twice) A purified and isolated RNA fragment that is conserved across at least two species comprising the sequence [NNUNNNNNNNGAUCNUNNNNNGAUNCUUUNUNNNAN(or absent)N(or absent)CCNNNNNNN (SEQ ID NO:20)] NNUNNNNNNNGAUCNUNNNNNGAUNCUUUNUNNNANCCNNNNNNN (SEQ ID NO:20), NNUNNNNNNNGAUCNUNNNNNGAUNCUUUNUNNNANCCNNNNNNN (SEQ ID NO:415) or NNUNNNNNNNGAUCNUNNNNNGAUNCUUUNUNNNACCNNNNNNN (SEQ ID NO:416).